



P/546-279 REISSUE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Reissue Patent Application of:

William Stern

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For : NASAL CALCITONIN FORMULATION

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Commissioner for Patents

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DECLARATION OF INVENTOR
WILLIAM STERN UNDER 37 CFR §1.1312

I, William Stern, hereby declare that:

1. I am the inventor named in the above-identified patent application, and am familiar with its contents.
2. Since 1991, I have been a Senior Research Scientist in the Protein Biochemistry Department at Unigene Laboratories, Inc. located in Fairfield, New Jersey. I was a Senior Scientist in the Protein Biochemistry Department at Unigene Laboratories from 1986 to 1990.
3. I received a Ph.D. in Biological Chemistry from the University of

Michigan in 1972.

4. I have read and am familiar with (1) the Office Action mailed on February 11, 2005 by the Examiner in charge of the above-identified patent application and (2) the prior art references cited therein. I make this Declaration in support of the patentability of the claimed invention.

5. The experiments and computations described herein, and as set forth in Table 1 attached hereto, were either performed by me or at my direction and under my supervision. Those experiments and computations involved determining the molar concentration of citric acid and citric acid salts in various examples set forth in the body of the following three references cited by the Examiner:

Grehow (U.S. Patent 5,026,825)
Kagatani (U.S. Patent 4,788,221)
Veronisi (U.S. Patent 6,107,277)

Additionally, because it is relevant to certain distinctions from the presently-pending patent claims, pH was determined in connection with several Grehow examples. The other references are believed distinguishable from the claims for reasons other than pH. Thus, pH was not determined for Veronisi or Kagatani. All results are reported in Table 1 attached hereto.

6. The specific examples analyzed in attached Table 1 were chosen by me as those which appeared most relevant, and closest in composition to the presently-claimed invention. Similar analysis of other examples can be made if the Examiner should deem it necessary.

7. Examples 7 and 10 of the Grehow reference, whose pH is reported in attached Table 1, indicate the presence of sodium phosphate, but do not state the type of sodium phosphate used (e.g., monosodium phosphate or disodium phosphate). Therefore, the solutions of each of examples 7 and 10 were prepared twice, once using monosodium phosphate and once using disodium phosphate. The pH of all four such solutions was measured and reported in

attached Table 1. Where Grebow examples stated % W/V, g/100ml was converted to mg/ml for consistency with the other examples in Table 1.

8. In the Kagatani reference, Table 1 attached hereto computes the citrate concentration for Kagatani's examples 1 and 4. In both of these examples, the citric acid concentration alone was too high to be within the scope of any of the pending patent claims. Additionally, sodium citrate was included in these examples which further increased the total citrate levels beyond the range claimed. It is pointed out that the extent of the hydration of the sodium citrate used in examples 1 and 4 in the Kagatani reference was not stated by Kagatani et al. For illustration purposes only, Table 1 assumes that the sodium citrate was a dihydrate form, but indicates with question marks that such assumption may not reflect what Kagatani et al. used. As pointed out, however, the hydration level of the Kagatani sodium citrate cannot affect my conclusion that citrate levels are beyond those set forth in the pending claims. None of the pending claims permit citrate higher than 50 mM. As noted above, the citric acid levels alone, in Kagatani's examples 1 and 4, provide citrate beyond this level. The additional sodium citrate (regardless of hydration) adds even more citrate and takes total citrate even farther beyond the claimed range.

9. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patents issued thereon.

8/10/05
Date

William Stern
William Stern

TABLE 1: DATA REFERENCED IN STERN DECLARATION

Patent	Example	Citric Acid			Na Citrate			Total Citrate		Sodium Phosphate		pH
		mg/ml	type	mM	mg/ml	type	mM	mM	mg/ml	mM	mg/ml	
Grebow	6	6	anhydrous	31.25	13.6	dihydrate	46.26	77.51	none	none	none	not determined
Grebow	7 (trial 1, assuming sodium phosphate is disodium phosphate)	3.4	anhydrous	17.71	none	none	none	17.71	24	169	7	
Grebow	7 (trial 2, assuming sodium phosphate is monosodium phosphate)	3.4	anhydrous	17.71	none	none	none	17.71	24	200	3.1	
Grebow	10 (trial 1, assuming sodium phosphate is disodium phosphate)	3.4	anhydrous	17.71	none	none	none	17.71	24	169	7	
Grebow	10 (trial 2, assuming sodium phosphate is monosodium phosphate)	3.4	anhydrous	17.71	none	none	none	17.71	24	200	3.1	
Grebow	13	12.19	monohydrate	58.05	12.37	dihydrate	42.07	100.12	none	none	none	not determined
Grebow	14	12.19	monohydrate	58.05	12.37	dihydrate	42.07	100.12	none	none	none	not determined
Veronesi	3	12.11	monohydrate	57.67	12.36	dihydrate	42.07	99.74	none	none	none	not determined
Veronesi	4	3.00	monohydrate	14.29	4.63	dihydrate	15.75	30.03	none	none	none	not determined
Kagazani	1	12.2	monohydrate	58.10	12.4	dihydrate***	42.07	100.17	none	none	none	not determined
Kagazani	4	12.2	monohydrate	58.10	12.4	dihydrate***	42.07	100.17	none	none	none	not determined

*assumed

